This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

MAY 14 2004
PATENT & TRADEMARK OFFICE

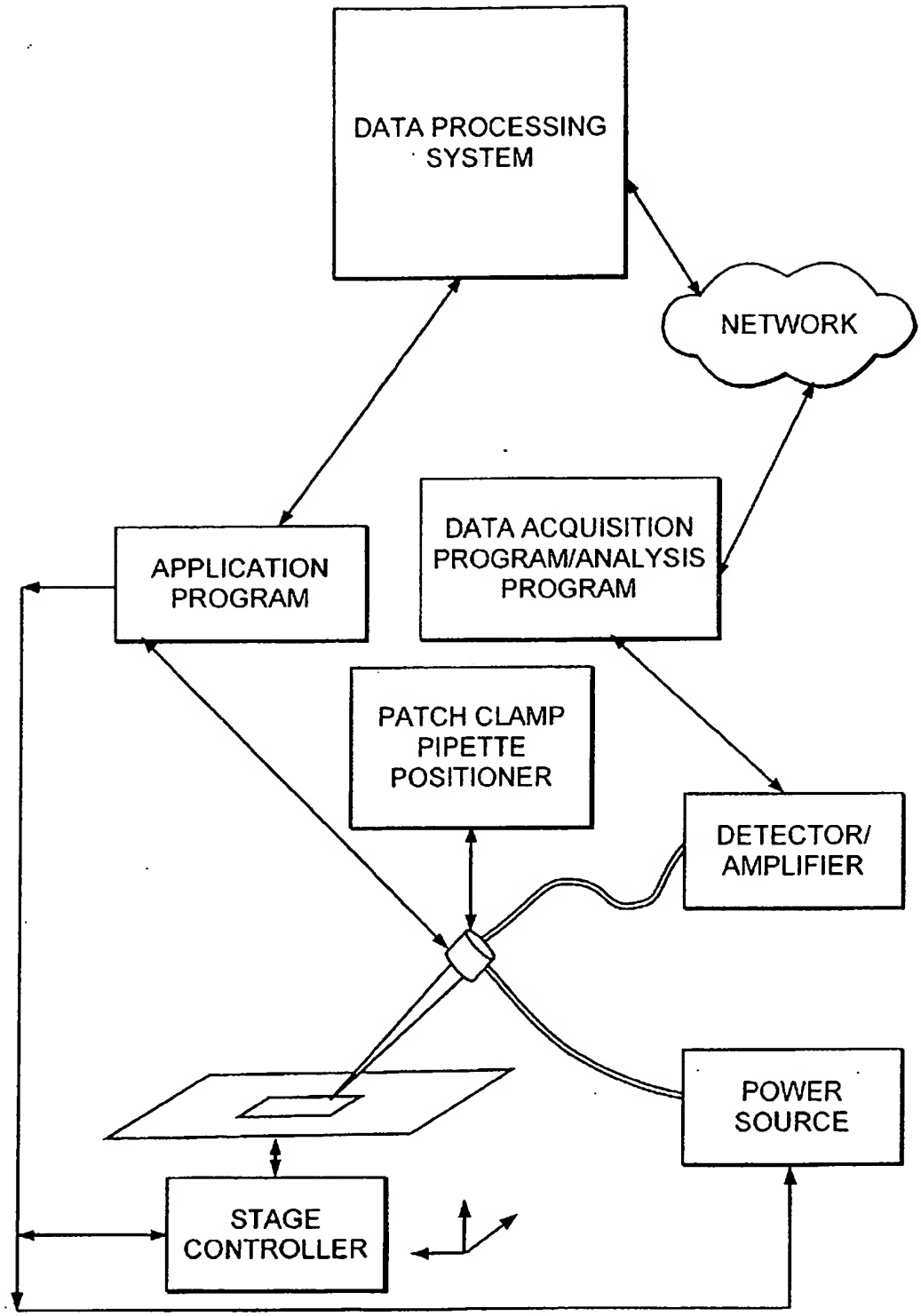


FIG. 1A

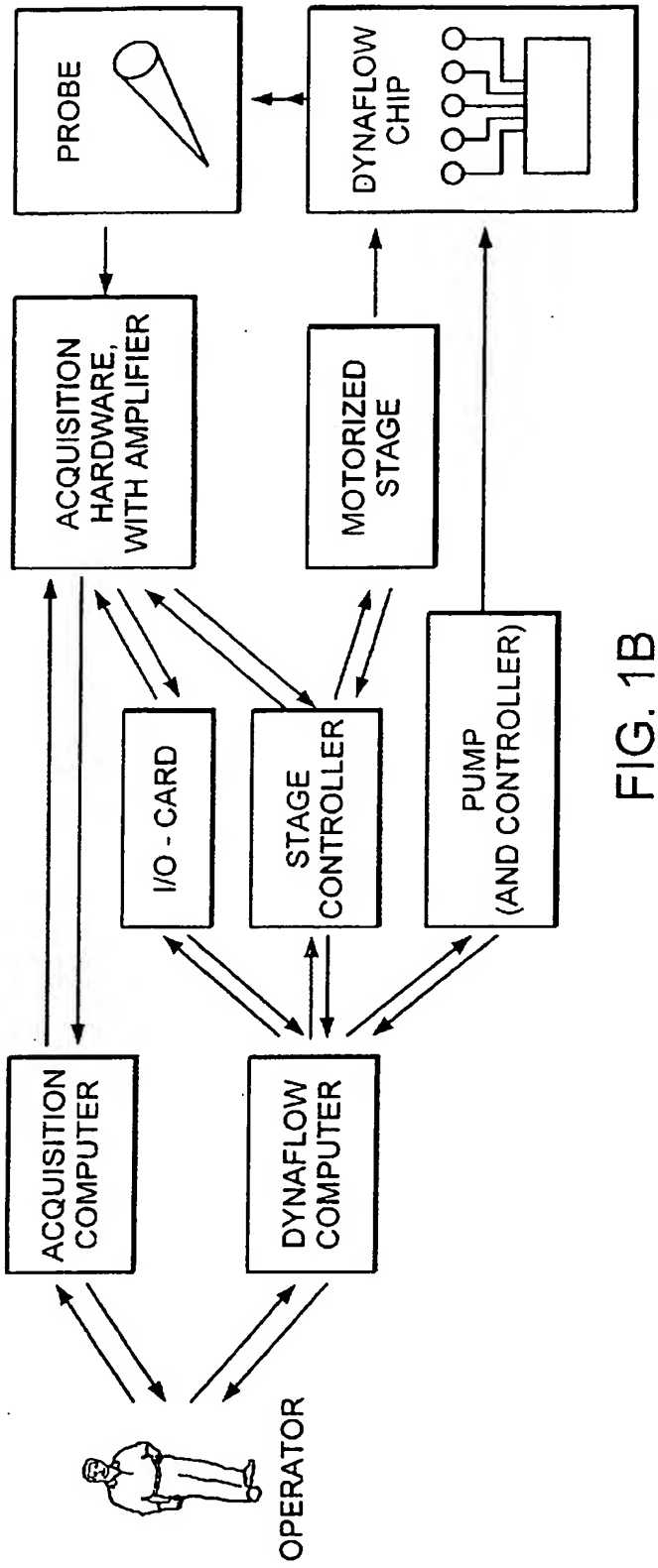

PROBE
DYNAFLOW CHIP
ACQUISITION HARDWARE, WITH AMPLIFIER
MOTORIZED STAGE
I/O - CARD
STAGE CONTROLLER
PUMP (AND CONTROLLER)
ACQUISITION COMPUTER
DYNAFLOW COMPUTER
OPERATOR

FIG. 1B

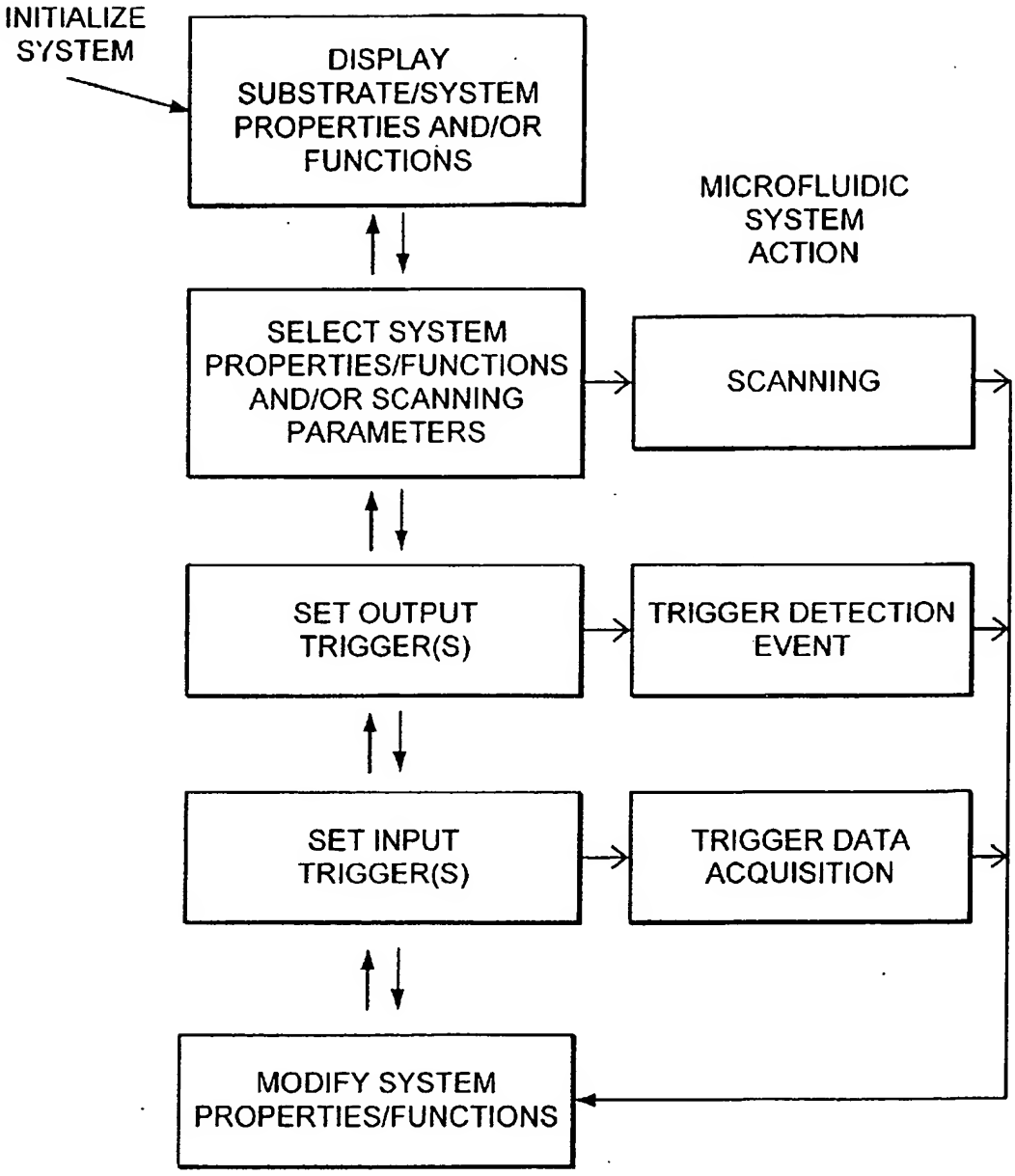

INITIALIZE SYSTEM
DISPLAY SUBSTRATE/SYSTEM PROPERTIES AND/OR FUNCTIONS
MICROFLUIDIC SYSTEM ACTION
SELECT SYSTEM PROPERTIES/FUNCTIONS AND/OR SCANNING PARAMETERS
SCANNING
SET OUTPUT TRIGGER(S)
TRIGGER DETECTION EVENT
SET INPUT TRIGGER(S)
TRIGGER DATA ACQUISITION
MODIFY SYSTEM PROPERTIES/FUNCTIONS

FIG. 1C

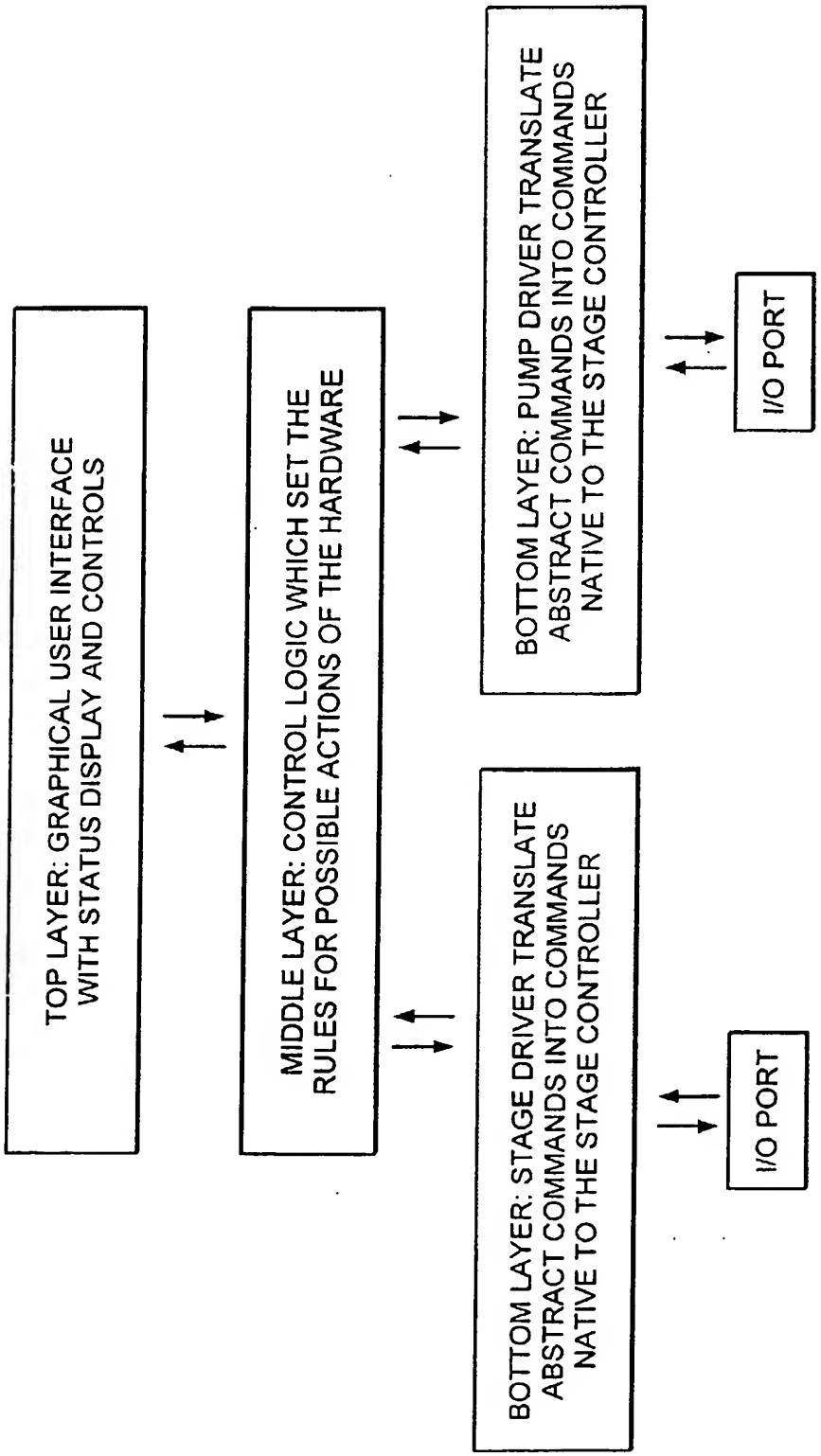

TOP LAYER: GRAPHICAL USER INTERFACE WITH STATUS DISPLAY AND CONTROLS
MIDDLE LAYER: CONTROL LOGIC WHICH SET THE RULES FOR POSSIBLE ACTIONS OF THE HARDWARE
BOTTOM LAYER: STAGE DRIVER TRANSLATE ABSTRACT COMMANDS INTO COMMANDS NATIVE TO THE STAGE CONTROLLER
I/O PORT
BOTTOM LAYER: PUMP DRIVER TRANSLATE ABSTRACT COMMANDS INTO COMMANDS NATIVE TO THE STAGE CONTROLLER
I/O PORT

FIG. 1D

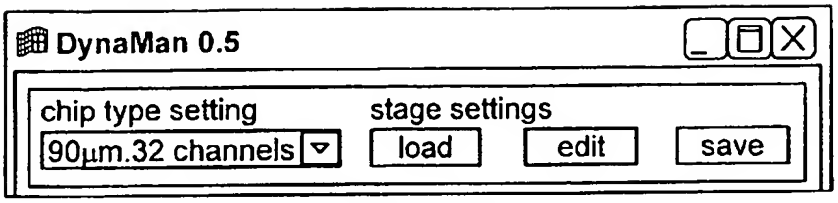
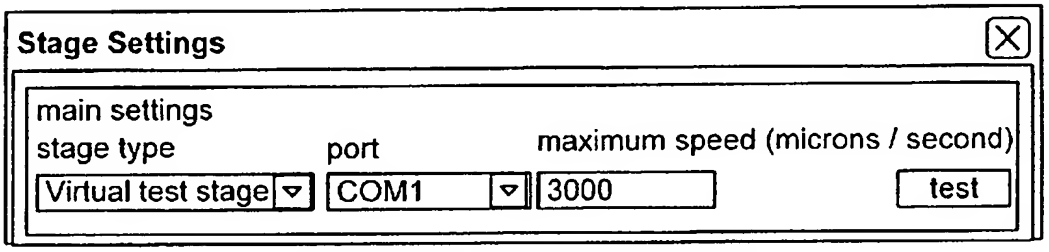
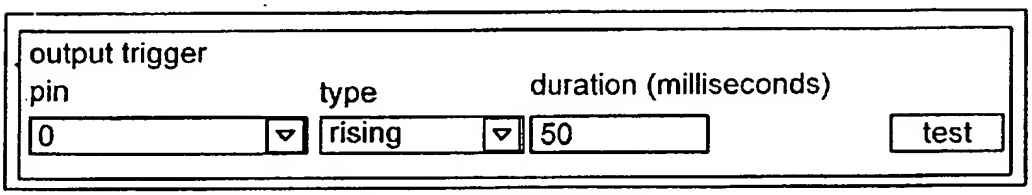


FIG. 2



Setting stage, port and max speed.

FIG. 3



Output trigger settings.

FIG. 4

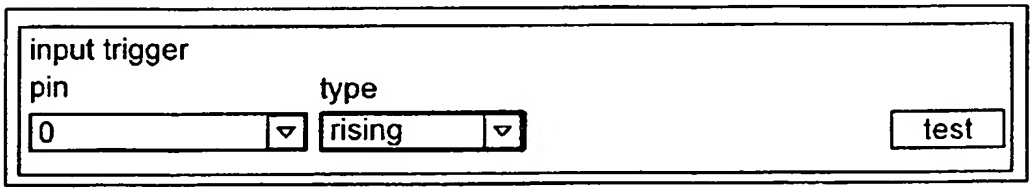


FIG. 5

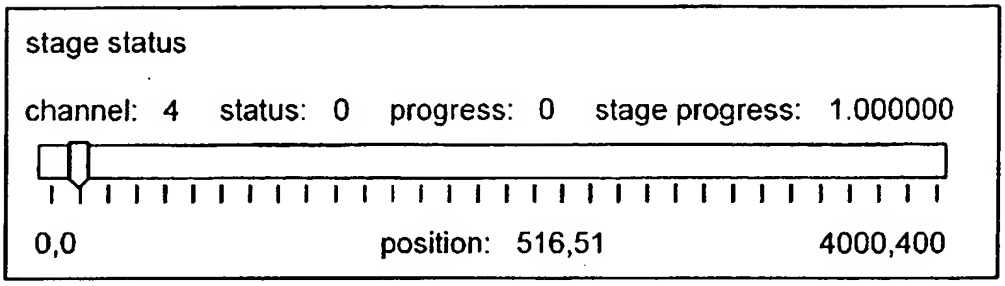

stage status
channel: 4 status: 0 progress: 0 stage progress: 1.000000
0,0
position: 516,51
4000,400

FIG. 6A

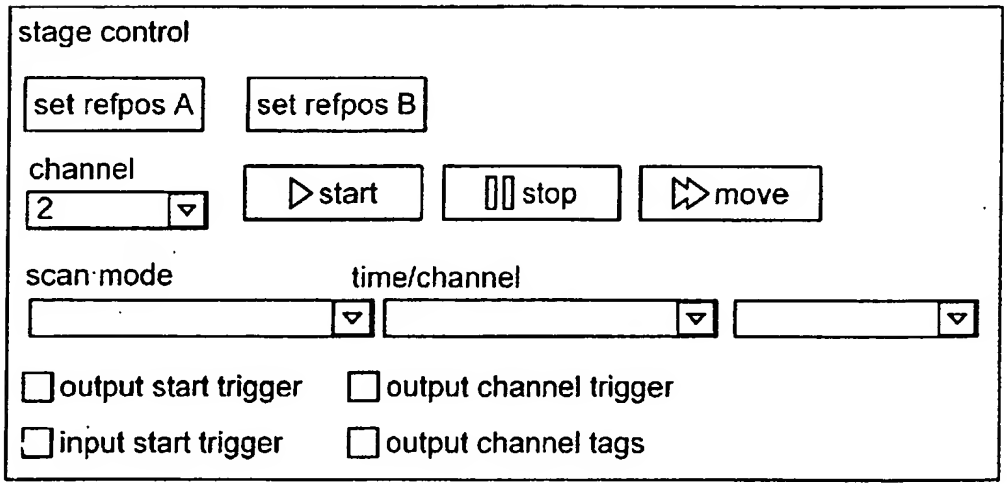

stage control
set refpos A
set refpos B
channel
2
start
stop
move
scan mode
time/channel
output start trigger
output channel trigger
input start trigger
output channel tags

FIG. 6B

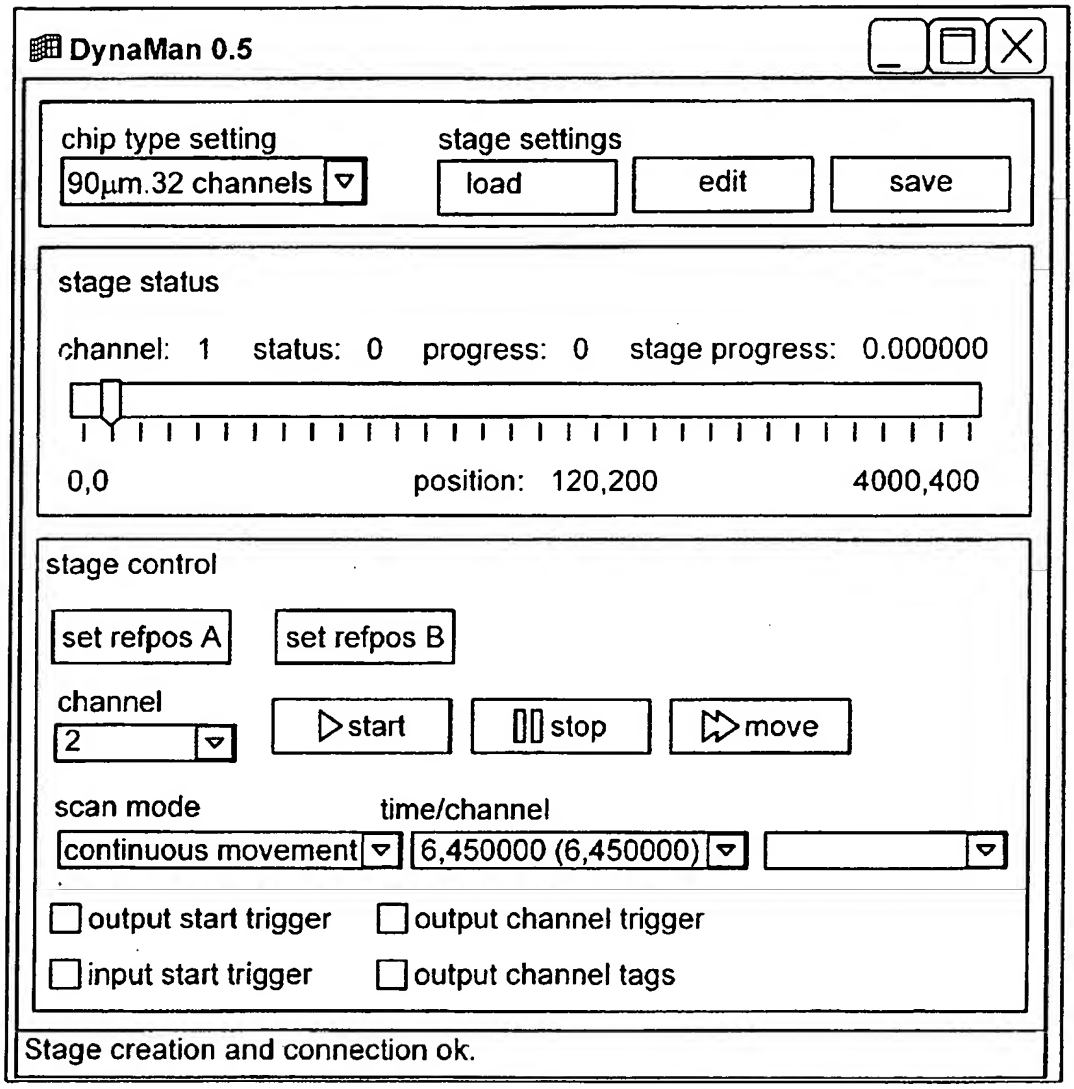

DynaMan 0.5
chip type setting
90µm.32 channels
stage settings
load
edit
save
stage status
channel: 1 status: 0 progress: 0 stage progress: 0.000000
0,0
position: 120,200
4000,400
stage control
set refpos A
set refpos B
channel
2
start
stop
move
scan mode
continuous movement
time/channel
6,450000 (6,450000)
output start trigger
output channel trigger
input start trigger
output channel tags
Stage creation and connection ok.

FIG. 7

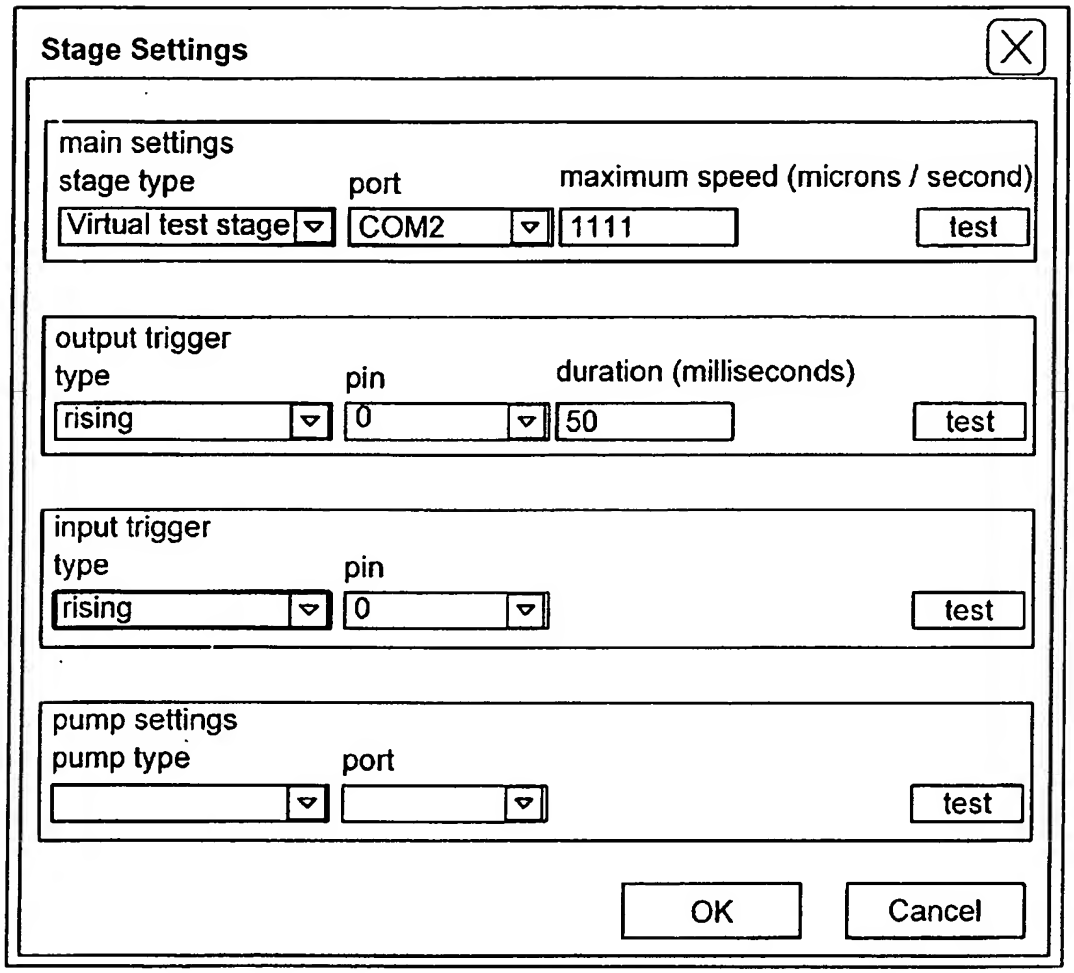

Stage Settings
main settings
stage type
port
maximum speed (microns / second)
Virtual test stage
COM2
1111
test
output trigger
type
pin
duration (milliseconds)
rising
0
50
test
input trigger
type
pin
rising
0
test
pump settings
pump type
port
test
OK
Cancel

FIG. 8

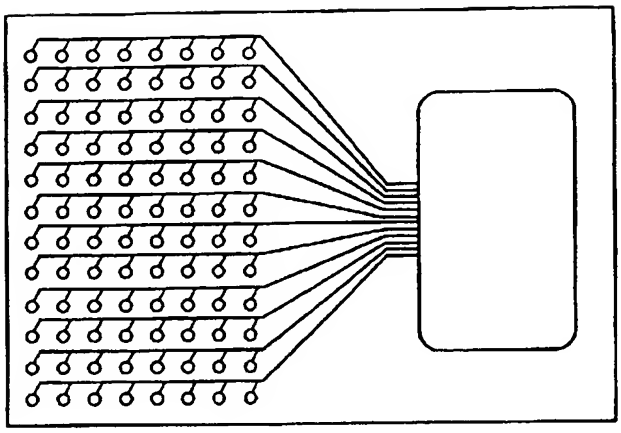


FIG. 9A

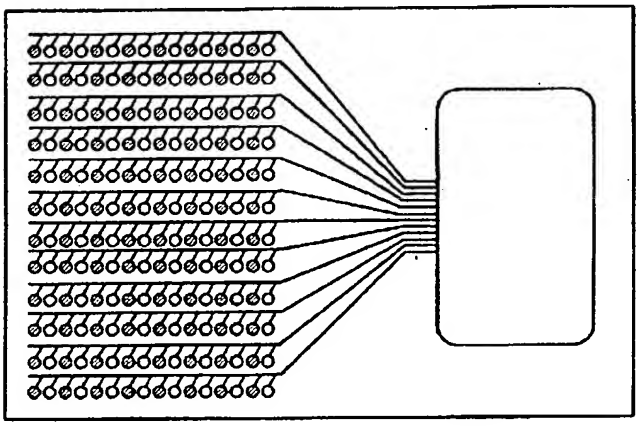


FIG. 9B

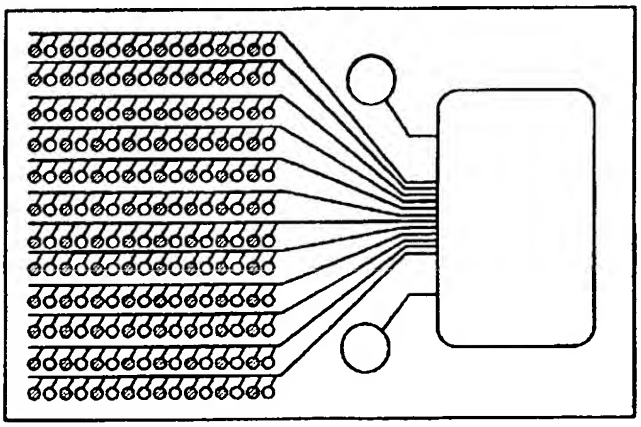


FIG. 9C

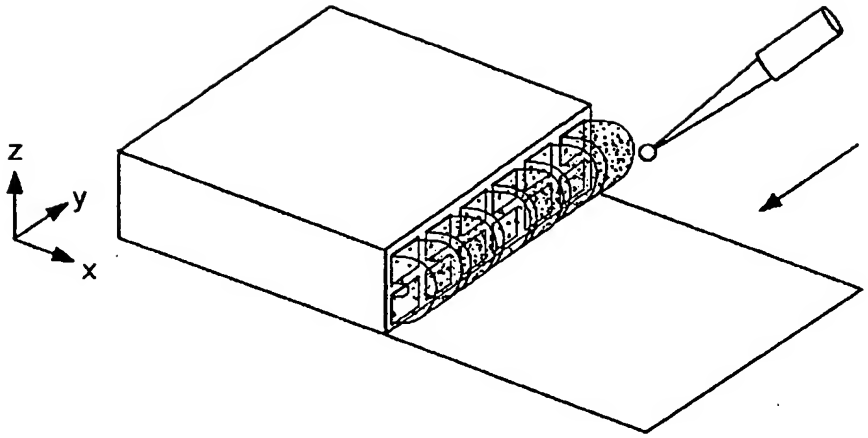


FIG. 10D

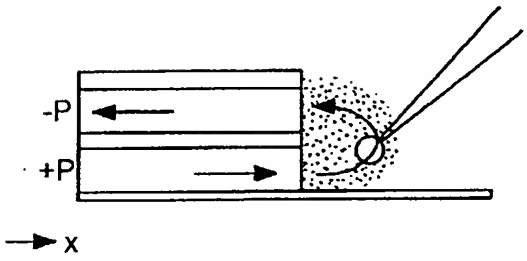


FIG. 10E

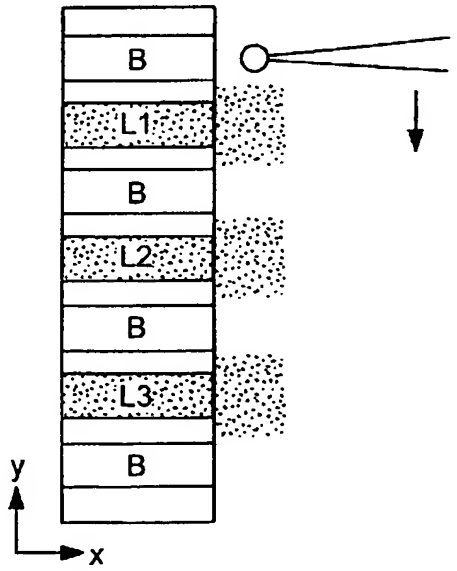


FIG. 10F

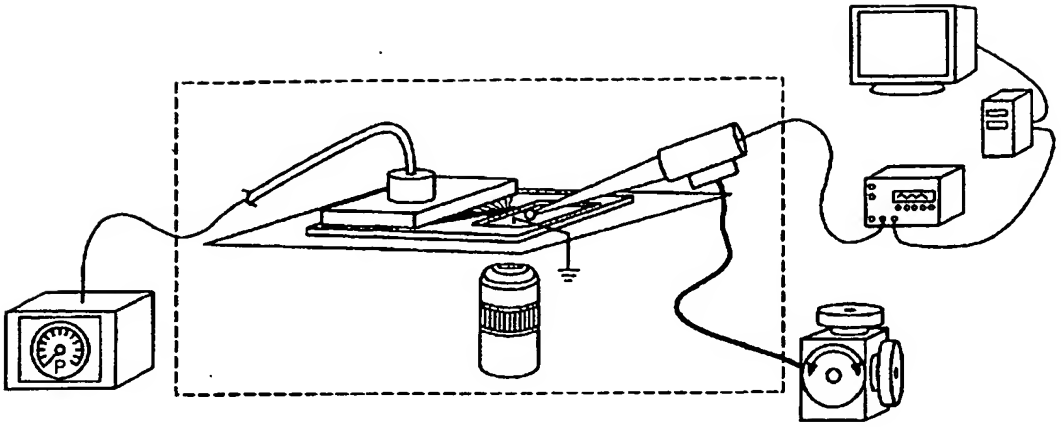


FIG. 11A

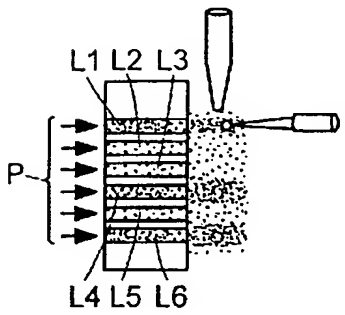


FIG. 11B

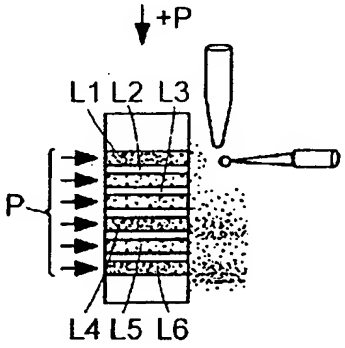


FIG. 11C

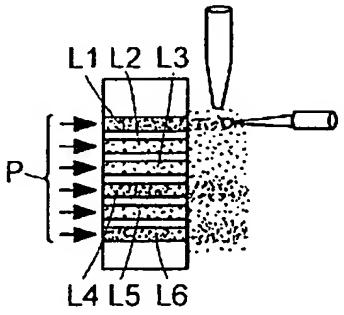


FIG. 11D

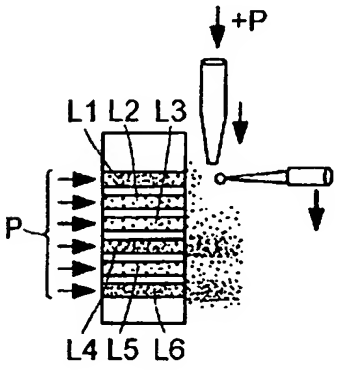


FIG. 11E

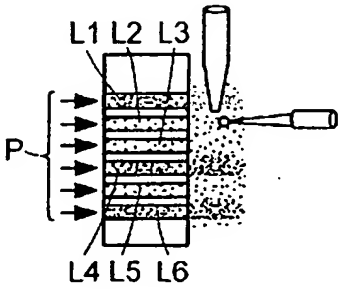


FIG. 11F

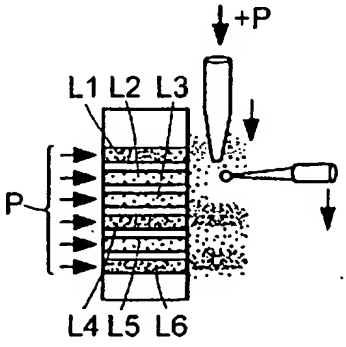


FIG. 11G

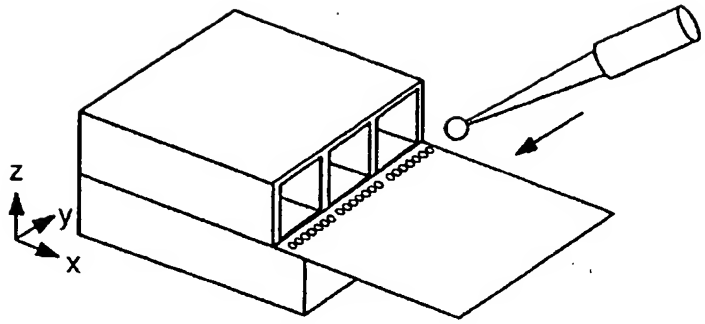


FIG. 11H

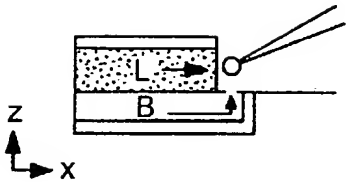


FIG. 11I

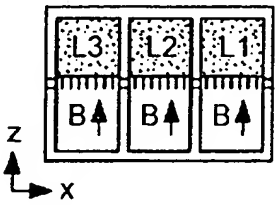


FIG. 11J

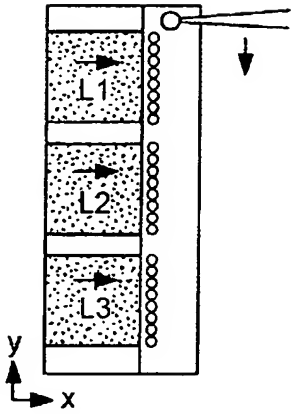


FIG. 11K

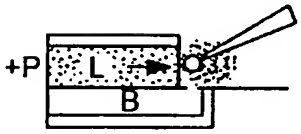


FIG. 11L

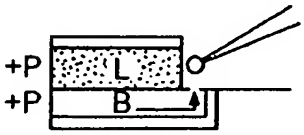


FIG. 11M

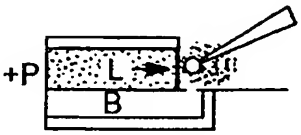


FIG. 11N

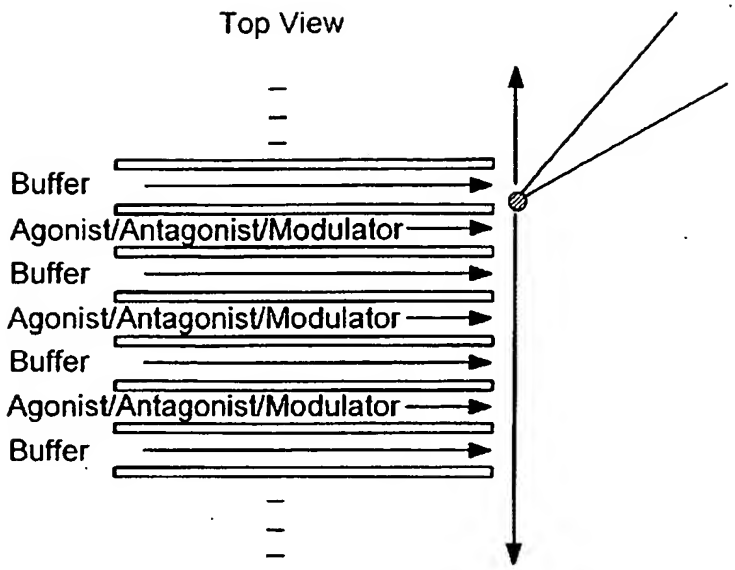


FIG. 12A

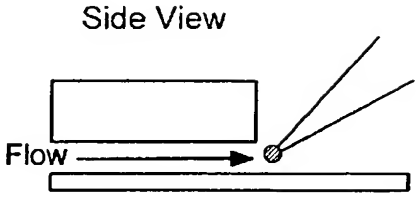


FIG. 12B

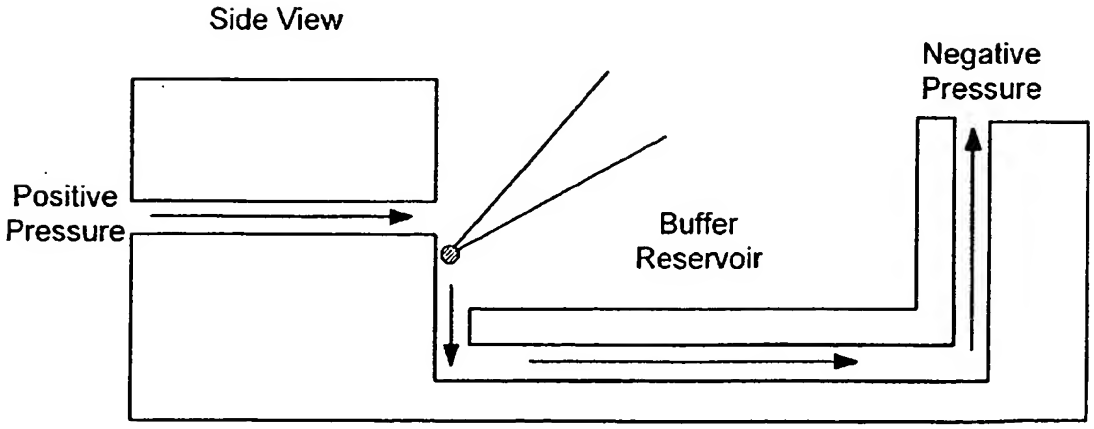


FIG. 12C

Channel content	B	T1	T2	T3	B	α1	B	α2	B	α3	B	α4	B	T2	B	α5	B	α6	B	α7	B	α8	B	T1	T2	T3
Channel #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26

FIG. 13A

Simulated trace for a single forward scan across microfluidic channel outlets:

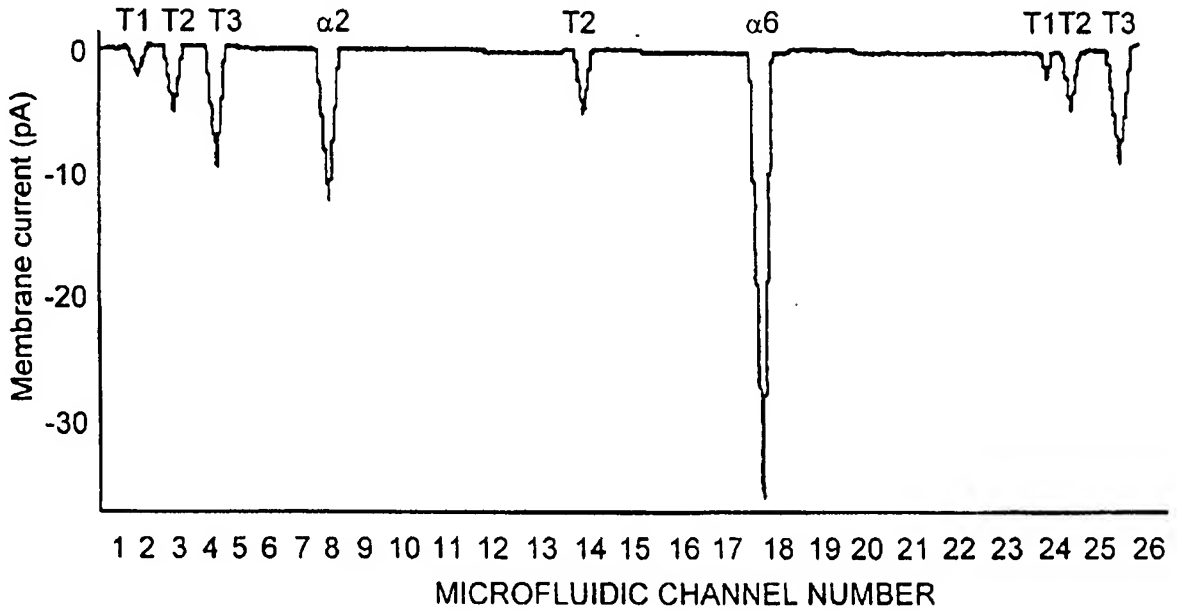


FIG. 13B

Score sheet (mean peak current amplitude of 6 scans)

Receptor response	0	1	5	10	0	0	0	12	0	0	0	0	0	5	0	0	0	37	0	0	0	0	0	1	5	10
Channel #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26

B=Buffer solution
T1= Test compound with known efficacy (agonist) at low concentration
T2= Test compound with known efficacy (agonist) at medium concentration (close to EC_{50}-value)
T3= Test compound with known efficacy (agonist) at high concentration(saturating concentration).
α=agonist with unknown efficacy

FIG. 13C

Channel content	B	T1	T2	T3	α1	α2	α3	α4	α5	α6	α7	T1	T2	T3
Channel #	1	2	3	4	5	6	7	8	9	10	11	12	13	14

FIG. 14A

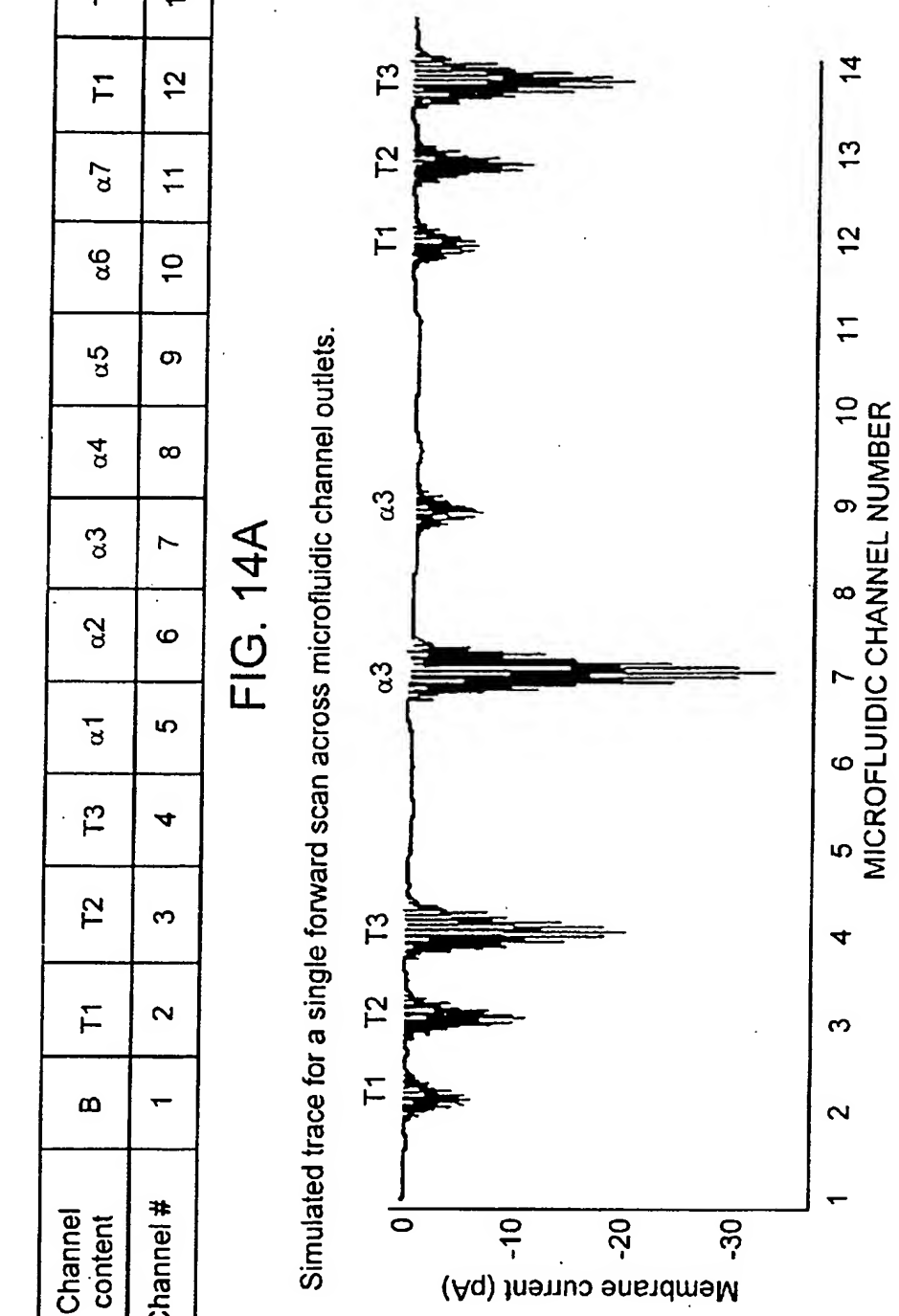


FIG. 14B

Score sheet (mean peak current amplitude of 6 scans)

Receptor response	0	5	10	20	0	0	34	0	4	0	0	5	10	20
Channel #	1	2	3	4	5	6	7	8	9	10	11	12	13	14

B = Buffer solution
T1 = Test compound with known efficacy (agonist) at low concentration
T2 = Test compound with known efficacy (agonist) at medium concentration (close to EC_{50}-value)
T3= Test compound with known efficacy (agonist) at high concentration(saturating concentration).
α = agonist with unknown efficacy

FIG. 14C

Content in channel	B	T1	T2	T 3	B	α1	B	α 2	B	α 3	B	α 4	B	T2	B	α 5	B	α 6	B	α7	B	α8	B	T1	T2	T3	B	α9
Channel #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Content in channel	B	T1	T2	T 3	α 20	B	α 19	B	α 18	B	α 17	B	α 16	B	α 15	B	T2	B	α 14	B	α 13	B	α 12	B	α 11	B	α 10	B
Channel #	56	55	54	53	52	51	50	49	48	47	46	45	44	43	42	41	40	39	38	37	36	35	34	33	32	31	30	29

FIG. 15A

Simulated trace for a single forward scan across microfluidic channel outlets:

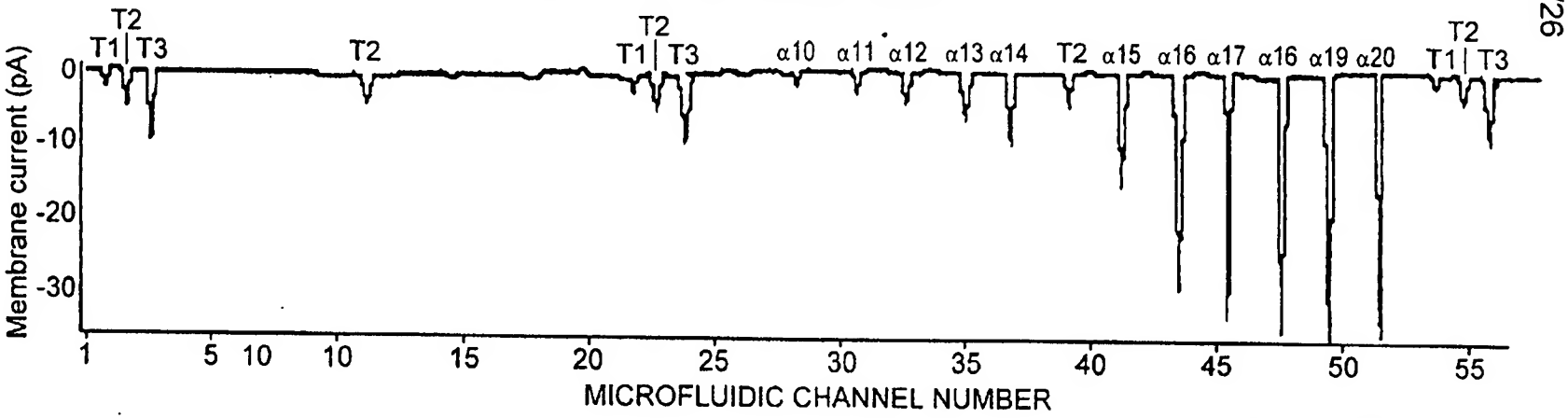


FIG. 15B

Score sheet (mean peak current amplitude of 6 scans)

Receptor response	0	1	5	10	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0	1	5	10	0	1
Channel #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Receptor response	0	1	5	10	36	0	35	0	32	0	27	0	24	0	15	0	5	0	12	0	8	0	6	0	3	0	2	0
Channel #	56	55	54	53	52	51	50	49	48	47	46	45	44	43	42	41	40	39	38	37	36	35	34	33	32	31	30	29

B = Buffer solution

T1= Test compound with known efficacy (antagonist or agonist) at low concentration

T2= Test compound with known efficacy (antagonist or agonist) at medium concentration (close to EC_{50}-value)

T3= Test compound with known efficacy (antagonist or agonist) at high concentration(saturating concentration).

α1-to-α28 agonist with unknown efficacy at different concentration progressively diluted(each step 10 times) to α1

FIG. 15C

Channel content	B + A	T 1+ A	T 2+ A	T 3+ A	B + A	A +ζ 1	B + A	A +ζ 2	B + A	A +ζ 3	B + A	A +ζ 4	B + A	T2 + A	B + A	A +ζ 5	B + A	A +ζ 6	B + A	A +ζ 7	B+ A	A+ ζ8	B+ A	T1	T2	T3
Channel #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26

FIG. 16A

Simulated trace for a single forward scan across microfluidic channel outlets:

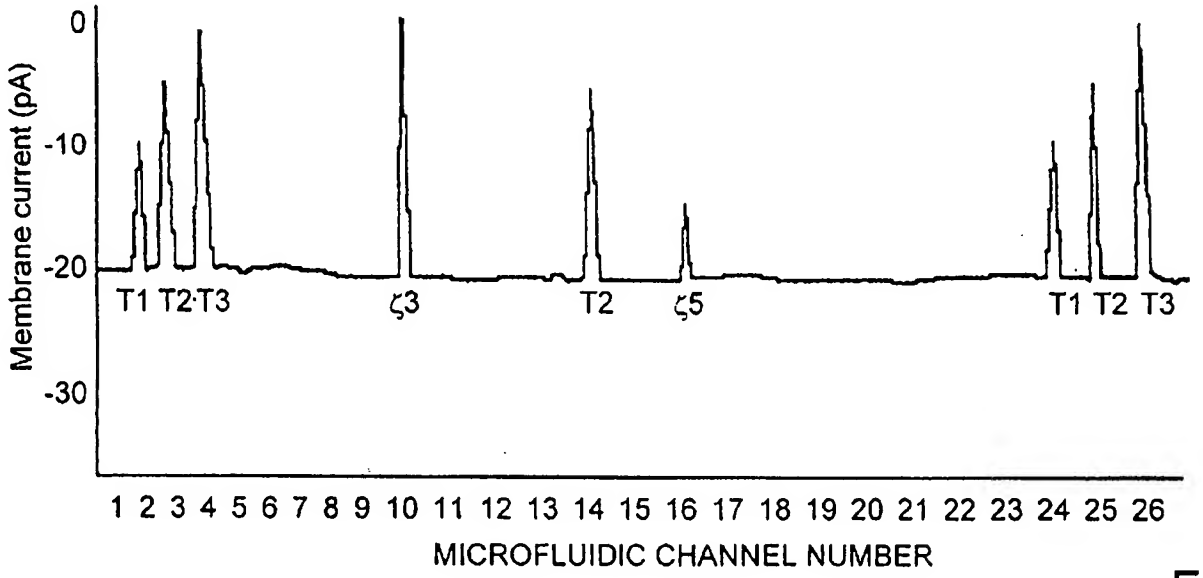


FIG. 16B

Score sheet (mean peak current amplitude of 6 scans)

Receptor response	20	10	5	1	20	20	20	20	20	1	20	20	20	5	20	15	20	20	20	20	20	20	20	10	5	1
Channel #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26

B=Buffer solution
T1= Test compound with known efficacy (antagonist) at low concentration
T2= Test compound with known efficacy (antagonist) at medium concentration (close to EC_{50}-value)
T3= Test compound with known efficacy (antagonist) at high concentration(saturating concentration).
A= agonist with known efficacy
ζ= antagonist with unknown efficacy

FIG. 16C

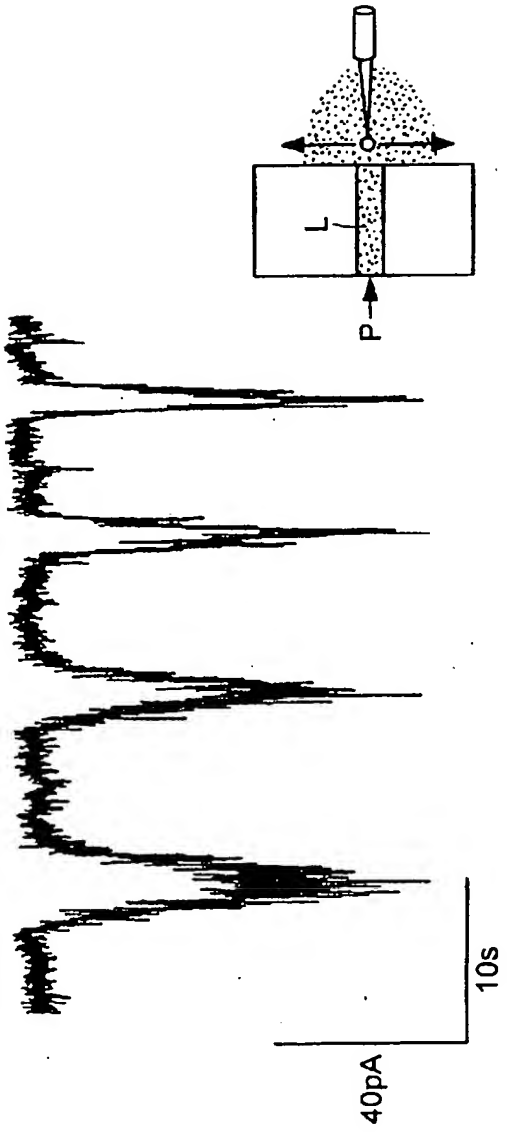


FIG. 17

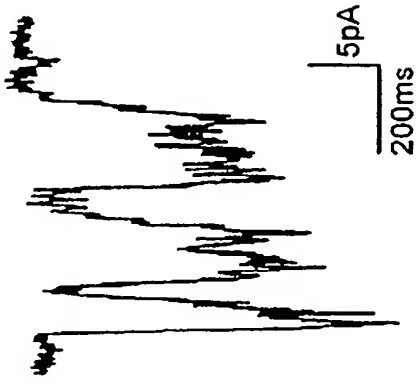


FIG. 18B

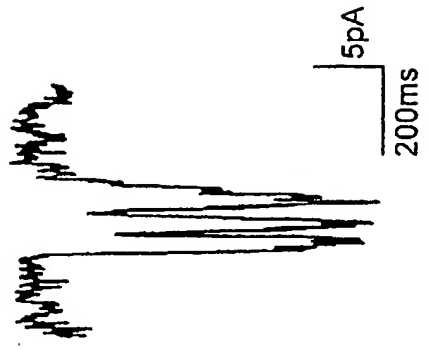


FIG. 18D

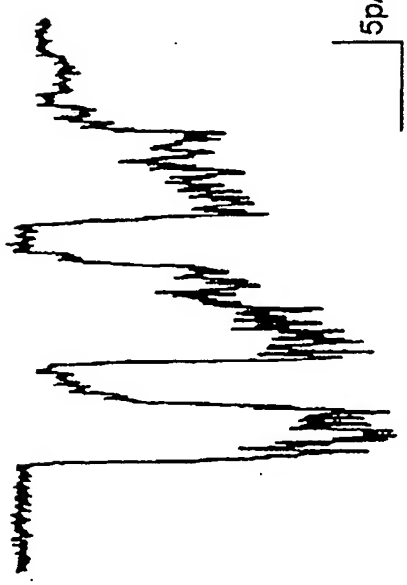


FIG. 18A

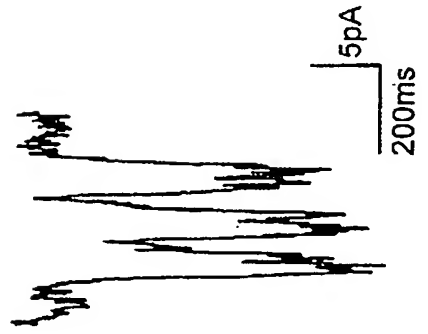


FIG. 18C

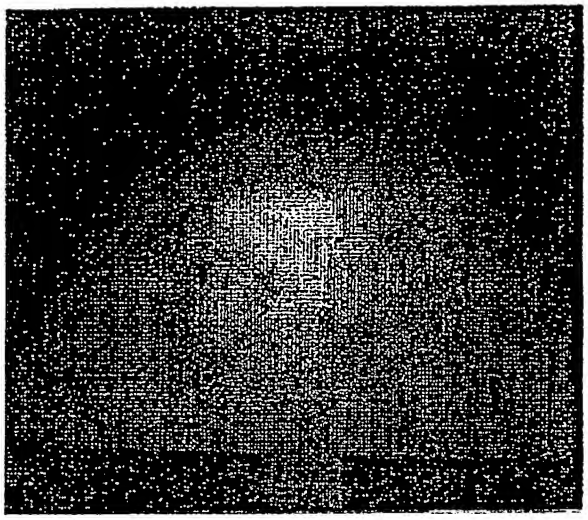


FIG. 19A

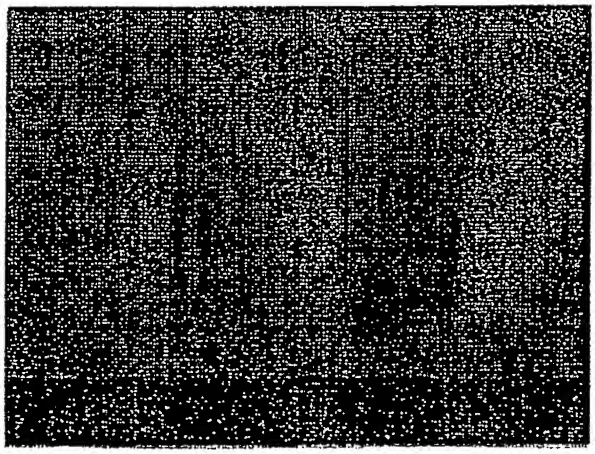


FIG. 19B

Current responses to 1 mM acetylcholine scan rate 16s/channel

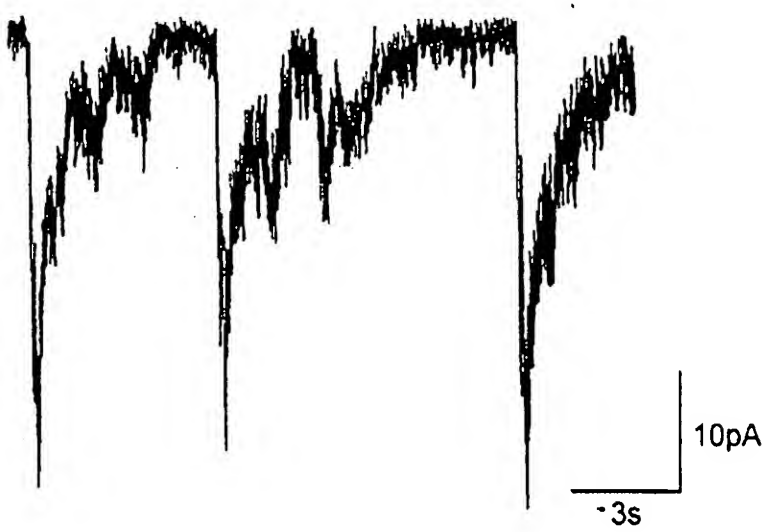


FIG. 20

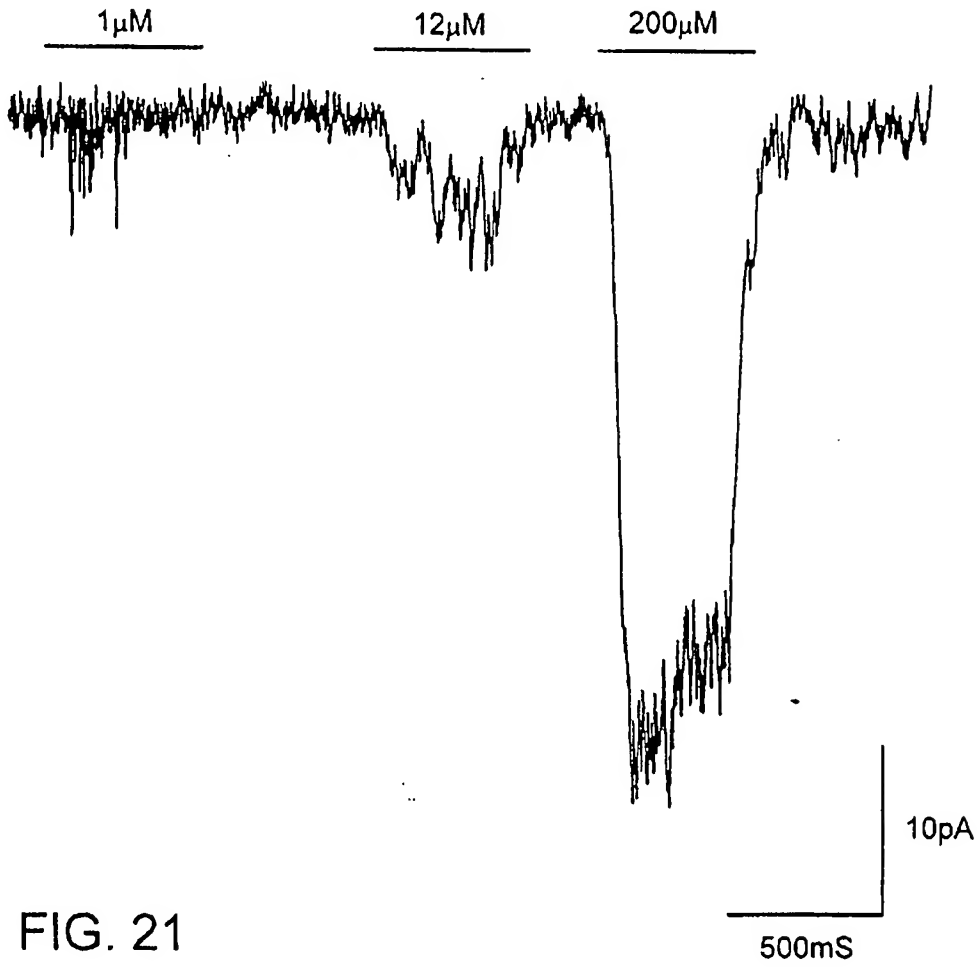


FIG. 21